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3-28-03

EV101936201US

Practitioner's Docket No. 2577/104

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Martyn Poliakoff, William Keith Gray, Thomas Macklyn Swan, Stephen Keith Ross, Stefan Wieland, and Stefan Roeder

Application No.: 09/914,699
Filed: 02/24/2000
For: Acid-Catalysed Reactions

Group No.: Not yet assigned
Examiner: Not yet assigned

**Commissioner for Patents
Washington, D.C. 20231**

EXPRESS MAIL CERTIFICATE

"Express Mail" label number EV 101936201 US
Date of Deposit 03/27/2003

I hereby state that the following *attached* paper or fee

1. Petition to Make Special;
2. Preliminary Amendment;
3. Certified copy of priority application GB 9904926.4; and
4. Return postcard.

is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 C.F.R. § 1.10, on the date indicated above and is addressed to the Commissioner for Patents, Washington, D.C. 20231.

Timothy M. Murphy

Signature of person mailing paper or fee

02577/00104 245510.1



DT20 Rec'd PCT/PTO 27 MAR 2003 PCT

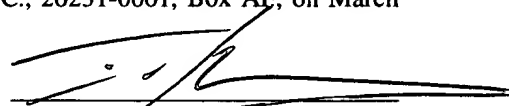
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Poliakoff, et al. Intl. Filing Date: February 24, 2000
Appl. No.: 09/914,699 Grp./Art Unit: Not yet assigned
Docket No: 2577/104 Examiner: Not yet assigned
Invention: ACID-CATALYSED REACTIONS

CERTIFICATE OF MAILING

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Timothy M. Murphy

EV 101936201 US
Express Mail Mailing Label Number

Honorable Commissioner of Patents
Washington, D.C. 20231

Petition to Make Special

[37 CFR § 1.102(d) and MPEP 708.02 VIII]

Sir:

In accordance with 37 CFR § 1.102(d), Applicants hereby petition to make special the above-referenced patent application. The petition is submitted herewith along with a check for \$130.00 for payment of the fee set forth in 37 CFR §1.17(h), as required by MPEP 708.02 VIII (A).

The PTO did not receive the following
listed item(s) check for \$130.00

Claims Directed to Single Invention/Prerequisite of Election Without Traverse

In compliance with the requirements of MPEP § 708.02 VIII (B), Applicants affirm that the application is directed to a single invention, as the application includes only a single independent claim. The invention can be broadly summarized as a continuous flow process in which acid-catalyzed reactions are performed at or near supercritical conditions in the presence of a heterogeneous acid catalyst. The acid-catalyzed continuous flow reaction process can lead to different products with high selectivity such as alkenes, ethers, acetals and ketals, merely by controlling the pressure, temperature, and flow rate of the continuous flow process.

In the event that the Examiner finds that the application is not obviously directed to a single invention, however, Applicants will make an election without traverse as a prerequisite of having the Petition to Make Special granted.

Statement of Pre-examination Search

In compliance with the requirements of MPEP § 708.02 VIII (C), Applicants affirm that a search of the relevant literature has been performed, as evidenced by the European Patent Office Search Report made in corresponding International Application No. GB9904926.4, a copy of which, along with the cited references as an IDS filed October 22, 2002, is submitted herewith as Appendix A.

Copy of References Most Closely Related

In compliance with the requirements of MPEP § 708.02 VIII (D), Applicants enclose copies of the references cited by the European Patent Office Search Report as relevant to the above-referenced application. The copies of these references are attached

herewith as Appendix A. Copies of these references were also included in the Information Disclosure Statement filed October 22, 2002.

Detailed Discussion of References

In compliance with the requirements of MPEP § 708.02 VIII (E), and 37 CFR § 1.111(b) and (c), Applicants provide herewith a detailed discussion of the references deemed most closely related to the subject matter encompassed by the claims of the above-referenced application.

Based on the International Search Report performed by the European Patent Office, the following references are discussed hereinbelow:

Ref. No.	Doc. No./ Journal	Iss/Publ'n Date	Inventor	Title
AA	US5,831,116	11/3/1998	Wang et al.	Catalytic Process for Making Ethers, Aldehydes, Esters and Acids from Alcohols Using a Supercritical Fluid Mobile
AB	EP652,202A1	5/19/1995	Ikariya et al.	A Method for Producing Formic Acid or its Derivatives
AC	Chemie Ingenieur Technik. Vol. 70, No. 12, 1998, pp. 1559-1563	Received 3/11/1998	Krammer et al.	Untersuchungen sum Synthesepotential in überkritischem Wasser
AD	J. Am. Chem. Soc.	Received 5/19/1999 Vol. 121, pp. 10711-10718	Gray et al.	The Continuous Acid-Catalyzed Dehydration of Alcohols in Supercritical Fluids: A New Approach to the Cleaner Synthesis of Acetals, Ketals, and Ethers with High Selectivity

AA. US5,831,116, Wang et al.

“Catalytic Process for Making Ethers, Aldehydes, Esters and Acids from Alcohols Using a Supercritical Fluid Mobile”

This patent discloses and claims a process for partially oxidizing alcohols such as methanol to the corresponding ether, aldehyde, ester or acid using a solid acid catalyst and oxygen in a supercritical fluid (SCF) mobile phase such as SCF CO₂. (See abstract.) In Wang et al., a single compound is converted into a corresponding single compound (aldehydes, esters and acids) by the *addition of oxygen* to the starting compound, or two molecules of the same alcohol, *with addition of O₂*, combine to form a symmetrical monoether. Suggested catalysts are those with redox functionality and Lewis acid and/or Brønsted acid sites to attract the reactant molecules and interact with oxygen, including transition metal oxides on solid supports such as silica, alumina, zirconia or TiO₂. Examples of disclosed preferred catalysts are oxides of Ti, Zr, V, Cr, Mn, Fe, Co, Ni, and Cu, particularly Fe₂O₃/TiO₂, Fe₂O₃/SiO₂, Cr₂O₃/Al₂O₃, Cr₂O₃/SiO₂, V₂O₅/SiO₂, NiO/Al₂O₃, NiO/SiO₂, and NiO/TiO₂. Every reaction disclosed in Wang et al. is an oxidation reaction.

In contrast, the present application is directed to a process for making ethers, acetals, ketals, and alkenes from mixed alcohols (including primary, secondary, and tertiary) and/or carbonyl compounds (including aldehydes and ketones) by means of *addition and subsequent dehydration*, using a heterogeneous catalyst under supercritical conditions or at near-critical conditions. Thus, claim 1 is directed to a single continuous flow reactor process which allows for synthesis of all the above-mentioned products through dehydration, merely by controlling T (temperature), P (pressure), and flow rate.

Furthermore, synthesis of diethers, or synthesis of an n,n-monoether from two n-alcohols with little or no rearrangement, or selective synthesis of a monoether from a polyol, are not disclosed or contemplated by the Wang et al. reference and are completely

surprising given that the knowledge generally available in the art suggests that synthesis of such ethers is not possible using an acid-catalyzed reaction.

For example, as stated in Volhardt's Organic Chemistry, 2nd Ed. (1994), W.H. Freeman and Company, p.295, last three lines, to p. 297, line 1, "In this [acid-catalyzed] reaction, the strongest nucleophile present in solution is the unprotonated starting alcohol. As soon as one alcohol molecule has been protonated, nucleophilic attack begins, the ultimate products being an ether and water. *Only symmetric ethers can be prepared by this method.*" Emphasis added.

None of the reactions of the present invention are oxidation reactions involving the addition of oxygen, they are all dehydration reactions. In fact, Wang et al. specifically distinguish their process for partially oxidizing alcohols to the corresponding ether from methods for preparing ethers by dehydration. (Column 1, lines 21-57.) Further, the Wang et al. reference does not disclose the synthesis of acetals and ketals, the synthesis of diethers, the surprisingly specific and efficient synthesis of a monoether from a polyol starting alcohol, the synthesis of n,n-monoethers from two n-alcohols, or the synthesis of alkenes, whereby all reactions are dehydration reactions, not oxidation reactions, and are performed using the same reaction process with the only variation being that of T, P, and/or flow rate.

Lastly, the reactions in Wang et al. are performed in an autoclave to increase both pressure and temperature to level high enough to reach a supercritical state (see Wang et al., col. 3, lines 41 – 65). Use of an autoclave means the reactions are batch reactions, which is incompatible with the concept of a continuous flow reactor, required in the present invention. In fact, it is a surprising and unexpected aspect of the present

invention that any degree of selectivity, let alone such a high degree as is seen, is obtained in a continuous flow system because the system is dynamic rather than static (as in the autoclave of Wang et al.), and dynamic systems tend to adversely affect selectivity.

For those reasons, Applicants respectfully submit that Wang et al. does not anticipate the present invention, nor render it obvious.

AB. EP652,202A1, Ikariya et al.

“A Method for Producing Formic Acid or its Derivatives”

This reference is directed to a method for producing formic acid or derivatives thereof, from supercritical carbon dioxide (scCO_2) reacting with an active hydrogen-containing compound such as H_2 , or compounds containing hydroxyl, carboxyl, carboxylamide, amino, imino, carbamate, urea, and vinyl groups. In this reference, the reaction may be accelerated in the presence of a metal catalyst, including a wide range of transition metal compounds, as either homogeneous or heterogeneous catalysts, but are preferably homogeneous catalysts soluble in scCO_2 . Furthermore, a preferred reaction scheme is one which employs a basic compound or mixture thereof. There is no suggestion in Ikariya et al. to make ethers, alkenes, acetals or ketals from alcohols in an acid-catalyzed reaction using a heterogeneous catalyst, or of making any products at all other than formic acid and formic acid derivatives from scCO_2 .

In contrast, the present invention is acid catalyzed, uses only a heterogeneous metal catalyst, is directed to the synthesis of mono- and diethers, alkenes, acetals and ketals from alcohols. It is not directed to making formic acid and derivatives thereof from scCO_2 , does not disclose the use of a homogeneous catalyst, and does not use CO_2 as a reactant in the disclosed reactions. As such, Applicants respectfully submit that Ikariya

et al. is merely tangentially related to the present application because of the terms supercritical fluid, metal catalysts, and alcohols, but is not substantively relevant for purposes of anticipating the presently claimed invention, or for purposes of rendering it obvious.

AC. Chemie Ingenieur Technik., (1998), Vol. 70, (12) pp. 1559-1563 Krammer et al.

“Untersuchungen sum Synthese-potential in überkritischem Wasser”

This article relates to the investigation and synthesis potential using supercritical water. Reactions investigated include: example 3 – the production of cyclic ethers from diols (dehydration of 1-4-butandiol); example 4 – alkenes and alkyl-carbonyls from polyols (dehydration of glycerol); example 5 – conversion of acetocyanohydrin into the corresponding acid salt, followed by elimination to the corresponding alkyl-acid salt; example 6 – decomposition of acetocyanohydrin into acetone, hydrogen cyanide, formamide, and peroxide; and example 7 – hydrolysis of esters (e.g. ethylacetate) into acetic acid, ethanol, and water. See Krammer et al., p. 1561, col. 1. In all cases, known simple reactions were investigated using scH_2O as the solvent, but none of the reactions involve a heterogeneous acid catalyst. In fact, the reaction of 1,4-hexanediol to make tetrahydrofuran is specifically done in the absence of an acid catalyst.

As with Ikariya et al., Applicants respectfully submit that Krammer et al. is merely tangentially related to the present application because of the terms supercritical, dehydration, and alcohols, but that it is not substantively relevant for purposes of anticipating the presently claimed invention, or for purposes of rendering the presently claimed invention obvious.

AD. J. Am. Chem. Soc., (1999), Vol. 121, pp. 10711-10718, Gray et al.

“The Continuous Acid-Catalyzed Dehydration of Alcohols in Supercritical Fluids: A New Approach to the Cleaner Synthesis of Acetals, Ketals, and Ethers With High Electivity”

This reference, which was “[r]eceived May 10, 1999” and “[p]ublished 11/06/1999,” and which has three authors in common with the Applicants, is not prior art to the presently claimed invention. The present application claims priority to March 4, 1999 from Great Britain National Application Serial No. GB/9904926.4. A certified copy of the priority document is enclosed herewith as Appendix B for verification of the priority date.

CONCLUSION

For the reasons set forth above, it is submitted that all pending claims are in condition for allowance. Consideration of the claims and a notice of allowance are therefore requested.

Please charge deposit account 19-4972 in the amount of \$130.00, as required by 37 CFR § 1.17(h) for a Petition to Make Special. Applicants believe that no additional fees are required. However, in the event that additional fees are owed and have been overlooked, please pay any fees additional fees required for the timely consideration of this application from deposit account number 19-4972. The Examiner is requested to telephone the undersigned if any matters remain outstanding so that they may be resolved expeditiously.

Date: March 27, 2003

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'Timothy M. Murphy', with a long horizontal flourish extending to the right.

Timothy M. Murphy
Registration No. 33,198
Attorney for Applicants
Bromberg & Sunstein LLP
125 Summer Street
Boston, Massachusetts 02110-1618
Tel: 617/443-9292
Fax: 617/443-0004

02577/00104 238362.2

APPENDIX A

IDS filed October 22, 2002

Docketed

FILE COPY

(Rel. 85-11/00 Pub.605)

FORM 6-1

6-17



Practitioner's Docket No. 2577/104

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent application

of _____

Inventor(s)

for _____

Title of invention

OR

In re application of: Poliakoff et al.

Application No.: 09/914,699

Group Art Unit: Not yet assigned

Filed: August 31, 2002

Examiner: Not yet assigned

For: Acid-Catalysed Reactions

Commissioner for Patents

Washington, D.C. 20231

INFORMATION DISCLOSURE STATEMENT

CERTIFICATE UNDER 37 C.F.R. § 1.8(a) and 1.10*

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- ☐ transmitted by facsimile to the Patent and Trademark Office.

Date: October 22, 2002

Signature _____

Timothy M. Murphy

(type or print name of person certifying)

(Information Disclosure Statement [6-1]--page 1 of 8)

NOTE: "An information disclosure statement shall be considered by the Office if filed by the applicant within any one of the following time periods:

- (1) Within three months of the filing date of a national application other than a continued prosecution application under § 1.53(d);
- (2) Within three months of the date of entry of the national stage as set forth in § 1.491 in an international application;
- (3) Before the mailing date of a first Office action on the merits; or
- (4) Before the mailing date of a first Office action after the filing of a request for continued examination under § 1.114."

37 C.F.R. § 1.97(b).

NOTE: "Each individual associated with the filing and prosecution of a patent application has a duty of candor and good faith in dealing with the Office, which includes a duty to disclose to the Office all information known to that individual to be material to patentability as defined in this section." 37 C.F.R. § 1.56(a).

"Individuals associated with the filing or prosecution of a patent application within the meaning of this section are:

- (1) each inventor named in the application;
- (2) each attorney or agent who prepares or prosecutes the application; and
- (3) every other person who is substantively involved in the preparation or prosecution of the application and who is associated with the inventor, with the assignee or with anyone to whom there is an obligation to assign the application." 37 C.F.R. § 1.56(c).

NOTE: The "duty as described in § 1.56 will be met so long as the information in question was cited by the Office or submitted to the Office in the manner prescribed by §§ 1.97(b)-(d) and 1.98 before issuance of the patent." Notice of January 9, 1992, 1135 O. G. 13 -25 at 17.

WARNING: "No information disclosure statement maybe filed in a provisional application." 37 C.F.R. § 1.51(d).

List of Sections Forming Part of This Information Disclosure Statement

The following sections are being submitted for this Information Disclosure Statement:
(check sections forming a part of this statement: discard *unused* sections and number pages consecutively)

1. ☐ Preliminary Statements
2. ☐ FORMS PTO/SB/08A and 08B (formerly FORM PTO-1449)
3. ☐ Statement as to Information Not Found in Patents or Publications
4. ☐ Identification of Prior Application in Which Listed Information Was Already Cited and for Which No Copies Are Submitted or Need Be Submitted
5. ☐ Cumulative Patents or Publications
6. ☐ Copies of Listed Information Items Accompanying This Statement
7. ☐ Concise Explanation of Non-English Language Listed Information Items
 - 7A. ☐ EPO Search Report
 - 7B. ☐ English Language Version of EPO Search Report
8. ☐ Translation(s) of Non-English Language Documents
9. ☐ Concise Explanation of English Language Listed Information Items (Optional)
10. ☐ Identification of Person(s) Making This Information Disclosure Statement

(complete the following, if appropriate)

Sections _____, respectively, have been continued on ADDED PAGE(S).

NOTE: "Once the minimum requirements are met the examiner has an obligation to consider the information." Notice of April 20, 1992 (1138 O.G. 37-41, 37).

Section 1. Preliminary Statements

Applicants submit herewith patents, publications or other information, of which they are aware that they believe may be material to the examination of this application, and in respect of which, there may be a duty to disclose.

The filing of this information disclosure statement shall not be construed as a representation that a search has been made (37 C.F.R. § 1.97(g)), an admission that the information cited is, or is considered to be, material to patentability, or that no other material information exists.

The filing of this information disclosure statement shall not be construed as an admission against interest in any manner. Notice of January 9, 1992, 1135 O.G. 13-25, at 25.

SECTION 2. FORMS PTO/SB/08A and 08B (formerly Form PTO-1449)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE



Applicants: Poliakoff et al.

Attorney Docket: 2577/104

Serial No: 09/914,1699

Art Group Unit: Not yet assigned

Date Filed: August 31, 2001

Examiner Name: Not yet assigned

Invention: Acid-Catalysed Reactions

LIST OF PATENTS AND PUBLICATIONS FOR APPLICANTS'
INFORMATION DISCLOSURE STATEMENT

United States Patents

Examiner Initials	Reference Number	Document Number	Issue Date	Inventor	Class/Subclass
_____	AA	5,831,116	3 Nov. 1998	Wang et al.	560/239

Foreign Patent Documents

Examiner Initials	Reference Number	Document Number	Publication Date	Country
_____	AB	0 652 202 A1	10 May 1995	European

Other Documents

Examiner Initials	Reference Number	Author	Title of Article, Title of Item, Date, Page(s), Volume- Issue Number(s)
_____	AC	Krammer et al.	"Untersuchungen zum Synthesepotential in überkritischem Wasser", Chemie Ingenieur Technik, Vol. 70, No. 12, 1998, pages 1559-1563, XP-000791730.



Other Documents (continued)

Examiner Initials	Reference	Author	Title of Article, Title of Item, Date, Page(s), Volume- Number Issue Number(s)
_____	AD	Gray, William et al.	"The Continuous Acid-Catalyzed Dehydration of Alcohols in Supercritical Fluids: A New Approach to the Cleaner Synthesis of Acetals, Ketals, and Ethers with High Selectivity" J. Am. Chem. Soc. (1999), 121 (46), 10711-10718, XP000887316.

Examiner Signature: _____

Date Considered: _____

NOTE FOR EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance AND not considered. Include copy of this form with next communication to applicant.

(Page 5 of 8)

Section 6. Copies of Listed Information Items Accompanying This Statement

NOTE: 37 C.F.R. § 198(a)(2) requires that any information disclosure statement filed under § 1.97 shall include:

**A legible copy of.:*

- (i) Each U.S. patent application publication and U.S. and foreign patent;*
- (ii) Each publication or that portion which caused it to be listed,*
- (iii) For each cited pending U.S. application, the application specification including the claims, and any drawing of the application, or that portion of the application which caused it to be listed including any claims directed to that portion. . .*

Legible copies of all items listed in Forms PTO/SB/08A and 08B (formerly Form PTO-1449) accompany this information statement.

(complete the following, if applicable)

Exception(s) to above:

- ☐ Items in prior application, from which an earlier filing date is claimed for this application, as identified in Section 4.
- ☐ Cumulative patents or publications identified in Section 5.

**Section 7A. Concise Explanation of Non-English Language Listed
Information Items-EPO Search Report**

The relevance with respect to the following citations listed on Forms PTO/SB/08A and 08B (formerly Form PTO-1449):

are submitted on the basis of the accompanying:

(check the appropriate item)

- ☒ EPO search report that is in the English language,
- ☐ EPO search report that is not in the English language and that is accompanied also by an English language version of the EPO search report,

that issued on the corresponding European patent application.

International Search Report for International Application No. PCT/GB00/00673 filed on 25 February 2000 is referenced as AE.

Section 10. Identification of Person(s) Making This Information Disclosure Statement

The person making this statement is

(check each applicable item)

- (a) ☐ the inventor(s) who signs below

SIGNATURE OF INVENTOR

(type or print name of inventor who is signing)

- (b) ☐ an individual associated with the filing and prosecution of this application (37 C.F.R. § 1.56(c))

SIGNATURE OF INVENTOR

(type or print name of inventor who is signing)

- (c) ☒ the practitioner who signs below on the basis of the information:

(check each applicable item)

- ☐ supplied by the inventor(s).
- ☐ supplied by an individual associated with the filing and prosecution of this application. (37 C.F.R. § 1.56(c))
- ☒ in the practitioner's file.

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Tel. No.: 617/443-9292

Customer No.: 002101



SIGNATURE OF PRACTITIONER

Timothy M. Murphy

(type or print name of person certifying)

Bromberg & Sunstein LLP

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TMM/nsj

PLEASE DATE STAMP AND RETURN
The Commissioner for Patents has received from Bromberg & Sunstein LLP the following re:

Inventor: Pollakoff et al.

Docket No: 2577/104

Title: Acid-Catalysed Reactions

Art Unit: Not yet assigned

Serial/Patent No: 09/914,699

Examiner: Not yet assigned

Filing/Issue Date: August 31, 2002

Date: October 22, 2002

Express Mail No:

Documents:

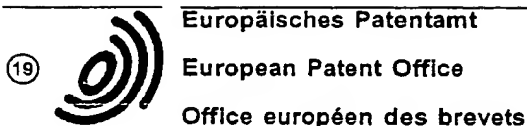
- | | |
|---|---|
| <input type="checkbox"/> New Application Transmittal | <input type="checkbox"/> Amendment Transmittal |
| <input type="checkbox"/> Provisional Application Cover Sheet | <input type="checkbox"/> Amendment (Preliminary) |
| <input type="checkbox"/> Description - _____ pages | <input type="checkbox"/> Response _____ |
| <input type="checkbox"/> Claims - _____ pages | <input checked="" type="checkbox"/> IDS & References AA-AE |
| <input type="checkbox"/> Abstract | <input type="checkbox"/> Petition for _____ month Extension |
| <input type="checkbox"/> _____ sheets of drawings
<input type="checkbox"/> formal <input type="checkbox"/> informal | <input type="checkbox"/> Transmittal of Formal Drawings |
| <input type="checkbox"/> Declaration & Power of Attorney
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BROMBERG & SUNSTEIN LLP

2577/104

125 SUMMER STREET BOSTON MA 02110-1618

Commissioner for Patents
Washington, DC 20231



11 Publication number : **0 652 202 A1**

12

EUROPEAN PATENT APPLICATION

21 Application number : **94308144.8**

22 Date of filing : **04.11.94**

51 Int. Cl.⁶ : **C07C 51/00, C07C 53/02,
C07C 67/00, C07C 69/04,
C07C 231/10, C07C 233/01**

- 30 Priority : **04.11.93 JP 274721/93
07.06.94 JP 125401/94
07.06.94 JP 125402/94**
- 43 Date of publication of application :
10.05.95 Bulletin 95/19
- 84 Designated Contracting States :
DE DK FR GB
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- 74 Representative : **Skailes, Humphrey John
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London WC2B 6UZ (GB)**

54 A method for producing formic acid or its derivatives.

57 Formic acid or derivatives thereof are produced from non-toxic carbon dioxide in the supercritical state, using it as raw materials, without using solvents, and at a high efficiency owing to a high reaction velocity, by reacting said carbon dioxide and an active hydrogen group-containing compound.

EP 0 652 202 A1

that use carbon monoxide.

For these reasons, the development of a new method to produce formic acid ester compounds which is simple to use, has an excellent productivity and a fast reaction rate is needed.

Formamide derivatives of formic acid, are also useful as basic raw materials in the organic chemical industry. They are extensively used in various industrial fields of chemicals, plastics, pharmaceuticals, agricultural chemicals, etc. Among others, N, N-dimethylformamide (DMF) is widely used as a polar solvent for synthesis reactions.

Conventional methods to produce these formamides include (1) a method to react an amine and carbon monoxide at a high temperature and under a high pressure using metal alkoxide catalysts (DMF Dimethyl formamide chemical uses, E. I. du Pont de Nemours, 1967, p217), (2) a method to react an amine and methyl formates in the atmosphere of carbon monoxide using a metal alkoxide catalyst (DMF Dimethyl formamide chemical uses, E. I. du Pont de Nemours, 1967, p217), and (3) a general method of reaction of a carboxylic acid, and carboxylic acid derivatives such as a carboxylic acid anhydride, a halide, or carbamate of carboxylic acid with amines (described in The Chemistry of Amides, J. Zabisky, or in EPA0 062 161 and DE2715044). Methods (1) and (2) above are used, for example, for the production of DMF for industrial use.

These conventional methods have their problems. For example, toxic carbon monoxide must be used at a high temperature and under a high pressure in the methods (1) and (2), or a high temperature is indispensable and the carboxylic acid derivatives, the main raw materials, must be separately synthesized in the methods (2) and (3).

Other known methods use less toxic carbon dioxide. In these methods, formamide derivatives are synthesized from carbon dioxide, hydrogen and an amine using metal complex catalysts. The catalysts used are 1) copper, zinc, cadmium, palladium or platinum halides or their phosphine or arsine complexes (U.S. patent 3 530 182), 2) phosphine complexes of cobalt, rhodium, iridium, and ruthenium (Tetrahedron Letters, 1970, No. 5, p365 or J. Mol. Catal, 1989, pL11), 3) phosphine complexes of ruthenium chloride (unscreened application 52-36617), 4) phosphine complexes of rhodium chloride and palladium chloride (Chem. Lett., 1977, p1495, or Bull. Inst. Chem. Res., Kyoto Univ., 1981, Vol. 59, p88) and 5) phosphine complexes of platinum (J. Chem. Soc., Chem. Commun., 1988, p602).

All of these known methods must use a large amount of solvent for reaction, and thus complicated procedures must be used to separate formic acid as the reaction product, from catalysts and solvents. Further, the reaction rate and the final yield of these methods are not high enough and thus these methods are not necessarily suitable for practical application.

For these reasons, the development of a new applicable method to produce formamide derivatives has an excellent productivity and a fast reaction rate is needed.

As described above in detail, formic acid and its derivatives have a large industrial value and fundamental improvements of the conventional production methods are strongly needed. So far, such improvements have never been reported.

SUMMARY OF THE INVENTION

The present invention was made to solve the above problems of the prior art, and provides a new method to produce formic acid or its derivatives from raw materials of low toxicity with a high reaction rate and featuring ease of operation and a satisfactory productivity.

To attain the above objects, the present invention provides a new method for producing formic acid or derivatives thereof by the reaction of carbon dioxide (CO₂) in the super critical state with an active hydrogen group-containing compound.

In the present invention, as described above, carbon dioxide (CO₂) in the super critical state react with hydrogen (H₂) as an active hydrogen group-containing compound, with an alcoholic compound (ROH), an amine compound (NR₁R₂R₃) or a carbamate compound, to produce formic acid, a formic acid ester, a formate, formamide and their derivatives.

BRIEF DESCRIPTION OF THE DRAWINGS

The attached Figure 1 shows the basic construction of a typical reaction system used in the production method according to the present invention. Figure 2 shows a typical arrangement of a reaction device in a continuous production method according to the present invention.

$\text{RuHCl}(\text{PMe}_3)_4$, $\text{RuH}(\text{CH}_3\text{COO})(\text{PMe}_3)_3$, $\text{RuH}(\text{HCOO})(\text{PMe}_3)_3$, $\text{RuH}_2(\text{PPh}_3)_4$, $\text{RuHCl}(\text{PPh}_3)_4$,
 $\text{RuH}(\text{CH}_3\text{COO})(\text{PPh}_3)_3$, $\text{RuH}_2(\text{PMe}_2\text{Ph})_4$, $\text{RuH}_2(\text{PMePh}_2)_4$, $\text{RuCl}_2(\text{PMe}_2\text{Ph})_4$, $\text{RuCl}_2(\text{PMePh}_2)_4$, $[\text{Ru}(\text{CO})_2\text{Cl}_2]_2$,
 $[\text{Ru}(\text{CO})_3\text{Cl}_2]_2$, $\text{Ru}_3(\text{CO})_{12}$, etc. The amount of the above-mentioned Group VIII metal complexes
 5 to be used in the present invention is not limited by a maximum or a minimum amount because the method
 according to the present invention does not use a solvent and depends on the productivity in the production
 of formic acid or its derivatives. Said amount is specified by the solubility in scCO_2 , size of autoclave, and econ-
 omy. The concentration of the catalyst or reaction accelerating agent is 50 to 5000 ppm, preferably 100 to 1000
 ppm by weight.

The use of a basic compound or mixture thereof is also effective in the present invention. Preferable basic
 10 compound is a nitrogen compound and the salt of the Group I metal in the periodic table. To be more specific,
 a nitrogen compound should be an amine compound specified by a generalized formula $\text{NR}^1\text{R}^2\text{R}^3$, preferably
 alkyl groups with the same or different R^1 , R^2 , and R^3 , or hydrogen. More preferable substances are mono-,
 di-, or tri-alkylamines where R^1 , R^2 , and R^3 are selected from the group comprising of hydrogen and C_1 to C_{10}
 15 alkyl group. Examples include ammonia, trimethylamine, triethylamine, tripropylamine, and tributylamine. The
 nitrogen compound could also be a cyclicamine. Amount of the nitrogen-containing basic substance is not par-
 ticularly limited, but should preferably be an amount which can be completely dissolved into scCO_2 to form a
 homogeneous phase. The adequate amount is 100 to 100,000 equivalents with respect to the catalyst or re-
 action accelerating agent, preferably 1,000 to 10,000 equivalents. Group I or II metal salt to be used includes
 20 a carbonate. The examples include Li_2CO_3 , LiHCO_3 , Na_2CO_3 , NaHCO_3 , K_2CO_3 , KHCO_3 , CaCO_3 , BaCO_3 , and
 SrCO_3 , preferably K_2CO_3 , Li_2CO_3 , and NaCO_3 . The metal salt is not soluble in scCO_2 , and thus any amount is
 employed, preferably in the 100 to 100,000 equivalents range with respect to the catalyst or reaction acceler-
 ating agent.

When producing formic acid by the reaction of supercritical carbon dioxide (scCO_2) and hydrogen, the fol-
 25 lowing conditions are employed in order that the reaction takes place preferably with the homogeneous phase
 in scCO_2 :

That is, carbon dioxide generally reaches its critical point at 72.9 atm pressure and 31°C temperature. The
 supercritical state is realized above this pressure and temperature level. The critical point for a mixture of car-
 bon dioxide and hydrogen gas is estimated from the research by C. Y. Tsang and W. B. Streett, Chem. Eng.
 Sci., Vol. 36, pp993-1000 (1981). According to their research, carbon dioxide should be in the 75 to 500 atm
 30 range, preferably 80 atm to 200 atm. The hydrogen gas pressure should be in the 20 to 150 atm range, pre-
 ferably 40 to 100 atm. The reaction temperature should be high enough for the reaction system to maintain
 the supercritical state, preferably between 40 and 120°C.

It is effective to add water or an alcohol compound to the reaction system. The amount should be in the
 10 to 10,000 equivalents range for the catalyst or reaction accelerating agent, preferably 10 to 1,000 equiva-
 35 lents. Reaction will take place in either the batch or the continuous method.

An alcohol compound is used as a raw material reaction agent in the production of formic acid ester. In
 this instance, the type of the alcohol compound is not particularly limited. Typical examples include primary
 alcohols and secondary alcohols. They may also be monohydric or polyhydric alcohols. Specifically, using the
 expression of ROH , R group may be selected from alkyl, cycloalkyl, phenyl, benzyl or other groups. Typical
 40 examples include methyl alcohol, ethyl alcohol, propyl alcohol, isopropyl alcohol, butyl alcohol, pentyl alcohol,
 hexyl alcohol, cyclohexyl alcohol, benzyl alcohol, etc. The amount to be used should be sufficient for these
 substances to be preferably completely dissolved into scCO_2 to form a homogeneous phase. The adequate
 amount is 100 to 100,000 equivalents for the catalyst or reaction accelerating agent, preferably 2,000 to 50,000
 equivalents.

45 The following are the suitable conditions for the reaction:

That is, carbon dioxide generally reaches its critical point at 72.9 atm pressure and 31°C temperature. The
 supercritical state is realized above this pressure and temperature level. The critical point for a mixture of car-
 bon dioxide and hydrogen gas is estimated from the research by C. Y. Tsang and W. B. Streett, Chem. Eng.
 Sci., Vol. 36, pp993-1000 (1981). According to their research, carbon dioxide should be in the 75 to 500 atm
 50 range, preferably 80 atm to 210 atm. The hydrogen gas pressure should be in the 20 to 150 atm range, pre-
 ferably 40 to 100 atm. The reaction temperature should be high enough for the reaction system to maintain
 the supercritical state, preferably between 40 and 120°C.

The reaction will take place whether the reaction type is the batch or the continuous method. The reaction
 time depends on the reaction type. For the batch method, the amine salt of the formic acid, the reaction inter-
 55 mediate, presents no problem even if it remains after the reaction because it is easily converted into carbon
 dioxide, hydrogen, and amine.

When producing a formamide, an amine compound or a carbamate compound must be used as a raw ma-
 terial for reaction.

Table 1

Test No	Catalyst (μmol)	NEt ₃ (mmol)	Pco ₂ (atm)	PH ₂ (atm)	Temp. (°C)	Time (hr)	Formic acid/ Catalyst (mole ratio)
Example 1	RuH ₂ (PMe ₃) ₄ 3.2	10	124	84	50	10	3700
Example 2	RuH ₂ (PMe ₃) ₄ 2.5	5	124	84	50	10	2500
Example 3	RuCl ₂ (PMe ₃) ₄ 3.2	5	124	84	50	10	2600
Example 4	RuCl ₂ (PMe ₃) ₄ 3.4	5	164	34	50	10	160
Example 5	RuCl ₂ (PMe ₃) ₄ 2.2	5	124	84	50	1	1040
Example 6	RuH ₂ (PMe ₃) ₄ 2.2	5	124	84	50	1	1400
Example 7	RuH ₂ (PMe ₃) ₄ 12.2	K ₂ CO ₃ 5	125	85	50	15	170

(Comparative Examples 1 to 5)

The reaction took place in the condition shown in Table 2.

The reaction rate was smaller than the working examples. The process to separate solvents was compli-

(Examples 8 to 14)

Formic acid was produced by the reaction in the same manner as Working Examples 1 through 7. 5.0 mmol triethylamine was present in the reaction. The reaction was conducted by coexisting water or methanol.

Hydrogen pressure was set in the 75 to 85 atm range so that the total pressure was in the 200 to 215 atm range. Reaction temperature was 50 °C, and the volume of the autoclave 50 ml.

The results are shown in Table 3.

As the table shows, the effect of addition of water or alcohol compounds is obvious.

were mixed at the ratio shown in Table 4, and charged into a stainless steel-made autoclave of internal volume 50 to 150 ml. Hydrogen gas pressure was increased to the specified level of 80 atm after argon substitution. The carbon dioxide pressure was increased to a specified level to reach the supercritical state and start reaction. After reaction, the yields of formate compounds, the product, were quantified by the above-mentioned method. The results are shown in Table 4.

The table shows that formic acid esters were produced at a high efficiency owing to a far greater reaction velocity than in the Comparative Example to be mentioned later.

Table 5

Test No.	$\text{RuCl}_2[\text{P}(\text{CH}_3)_3]_4$ (μmol)	Additive (mmol)	CH_3OH (mmol)	Temp. ($^\circ\text{C}$)	Time (hr)	Formic acid ester/ catalyst (mole ratio)	Formic acid/ catalyst (mole ratio)
Comparative Example 6	2.7	0	79.0	80	60	7	0
Comparative Example 7	3.2	n-Bu ₃ PO 0.72	13.3	80	15	7	0
Comparative Example 8	3.0	NEt ₃ 5	0	50	15	0	2600

(Example 21)

The reaction took place in the same manner as in Working Example 15 except that the quantity of the cat-

Table 6

Test No.	$\text{RuCl}_2[\text{P}(\text{CH}_3)_3]_4$ (μmol)	Amine Compounds	Temp. ($^{\circ}\text{C}$)	Time (hr)	DMF/catalyst (mole ratio)	Formic acid/ catalyst (mole ratio)
Example 23	2.4	Dimethylamine 1.7ml	100	20	14,500	0
Example 24	2.4	Dimethylamine 0.5ml	75	5	1,400	2,000
Example 25	2.5	carbamate 35.1mmol	100	20	25,400	275
Example 26	2.5	carbamate 87.7mmol	100	19	62,000	680
Example 27	2.4	carbamate 212mmol	100	18	156,000	4,000
Example 28	2.4	carbamate 280mmol	100	24	188,000	113
Example 29	2.4	carbamate 5.0mmol	100	1	2,600	3,500
Example 30	2.4	carbamate 5.0mmol	100	6	3,500	130
Example 31	2.5	carbamate 5.0mmol	100	1	1,040	1,600
Example 32	2.7	carbamate 576.0mmol	100	37	370,000	trace

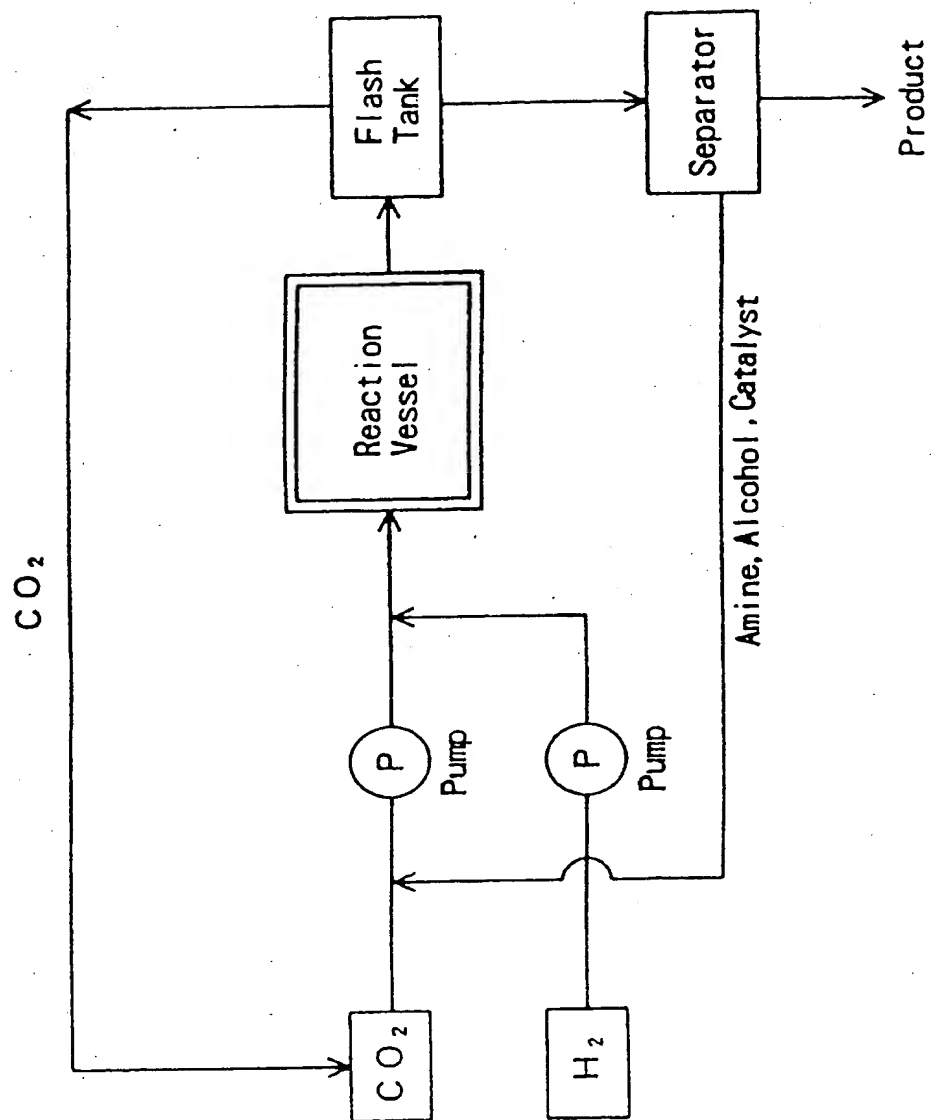
(Comparative Examples 9 and 10)

The reactions took place in the condition shown in Table 7. The table shows that the presence of a catalyst is essential. It also demonstrates that the reaction activity significantly decreases if THF is used as a solvent in comparative Example 10.

Claims

1. A method for producing formic acid or derivatives thereof by the reaction of carbon dioxide in the supercritical state with an active hydrogen group-containing compound or mixture thereof.
- 5 2. A method as claimed in claim 1 wherein said reaction takes place in the presence of a transition metal catalyst.
3. A method as claimed in claim 2 wherein said transition metal catalyst is selected from a group comprising of Group VIII transition metal compounds or complexes.
- 10 4. A method as claimed in claim 3 wherein said Group VIII transition metal is rhodium, palladium, ruthenium, iridium or platinum.
5. A method as claimed in claim 1 wherein said reaction takes place in the presence of a basic substance.
- 15 6. A method as claimed in claim 1 wherein said active hydrogen group-containing compound is hydrogen or a compound containing at least one active hydrogen group selected from hydroxyl group, carboxyl group, carboxylamide group, amino group, imino group, carbamate group, urea group, and vinyl group.
- 20 7. A method to produce formic acid by the reaction of carbon dioxide in the supercritical state with hydrogen in the presence of a transition metal compound or complex.
8. A method as claimed in claim 7 wherein said reaction takes place in the presence of a basic substance.
- 25 9. A method as claimed in claim 7 wherein said reaction takes place in the presence of an alcohol compound.
10. A method as claimed in claim 7 wherein said reaction takes place in the presence of a Group VIII transition metal compound or complex.
- 30 11. A method as claimed in claim 10 wherein said Group VIII transition metal is rhodium, palladium, ruthenium, iridium or platinum.
12. A method as claimed in claim 8 wherein said basic substance is a nitrogen-containing organic compound or the salt of Group I metal.
- 35 13. A method to produce formic acid ester compound by the reaction of carbon dioxide in the supercritical state with hydrogen and an alcohol compound in the presence of a transition metal compound or complex.
14. A method as claimed in claim 13 wherein said reaction takes place in the presence of a basic substance.
- 40 15. A method as claimed in claim 13 wherein said reaction takes place in the presence of a Group VIII transition metal compound or complex.
16. A method as claimed in claim 15 wherein said Group VIII transition metal is rhodium, palladium, ruthenium, iridium or platinum.
- 45 17. A method as claimed in claim 14 wherein said basic substance is a nitrogen-containing organic compound or the salt of Group I metal.
18. A method to produce formamide compound by the reaction of carbon dioxide in the supercritical state with hydrogen and ammonia, primary or secondary amine compound or carbamate compound corresponding thereto in the presence of a transition metal compound or complex.
- 50 19. A method as claimed in claim 18 wherein said reaction takes place in the presence of a compound or complex of a Group VIII transition metal.
- 55 20. A method as claimed in claim 19 wherein said Group VIII transition metal is rhodium, palladium, ruthenium, iridium or platinum.

FIG. 2





European Patent
Office

EUROPEAN SEARCH REPORT

Application Number
EP 94 30 8144

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
P, X	CHEMISTRY LETTERS, vol.1994, no.8, 1994 pages 1533 - 1536 MIZUNO, T ET AL. 'Photocatalytic Reduction of CO ₂ with Dispersed TiO ₂ /Cu Powder Mixtures in Supercritical CO ₂ ' -----	1-20	
			TECHNICAL FIELDS SEARCHED (Int.Cl.6)
The present search report has been drawn up for all claims			
Place of search MUNICH		Date of completion of the search 30 January 1995	Examiner Janus, S
CATEGORY OF CITED DOCUMENTS		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons ----- & : member of the same patent family, corresponding document	
X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document			

EPO FORM 1500 (3.92) (P04/C01)

Literatur

- [1] LEGRINI, O.; OLIVEROS, E.; BRAUN, A. M.
Chem. Rev. 93 (1993) S. 671/698.
- [2] KÖPPKE, K.-E.
Korrespondenz Abwasser 40 (1993) S. 62/67.
- [3] YADEGARDJAM, F.; LUFT, G.; BAUR, K.; GREGOR, K.-H.
Wasser Luft Boden 39 (1995) S. 36/38.
- [4] SCHWARZ, H.; LUFT, G.; BAUR, K.; GREGOR, K.-H.
Wasser Luft Boden 40 (1996) S. 44/47.
- [5] SCHRÖDER, H. F.
Korrespondenz Abwasser 39 (1992) S. 387/394.
- [6] STOFFLER, B.
Dissertation, TU Darmstadt 1997.
- [7] YADEGARDJAM, F.
Dissertation, TH Darmstadt, 1995.
- [8] BUXTON, G. V.; GREHNSTOCK, C.; HELMAN, W. P.;
ROSS, A. B.
J. Phys. Chem. Ref. Data 17 (1988) S. 513-759.

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Untersuchungen zum Synthesepotential in überkritischem Wasser

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 UND HERBERT VOGEL

p. 1559-1563 = (5)
 p. d. 12-1998

1 Problemstellung

Wasser spielt bei vielen chemischen Reaktionen als Lösungsmittel, Reaktionspartner und Katalysator eine wichtige Rolle. Es ist billig, nicht toxisch, weder brennbar noch explosiv und umweltverträglich. Reaktionen in Wasser tragen somit zur Abfallvermeidung und Ressourcenschonung bei. Viele organische Substanzen reagieren allerdings bei niedrigen Temperaturen nicht oder nur ungenügend in bzw. mit Wasser. Dieses Verhalten ändert sich jedoch dramatisch bei Temperaturerhöhung, hier zeigt sich Wasser als äußerst reaktiver Partner. Insbesondere in der Nähe des kritischen Punktes können die Eigenschaften der wässrigen Reaktionsmischung (z. B. Dichte, Löslichkeiten, Dielektrizitätskonstante, Ionenprodukt, Wärmekapazität und Transporteigen-

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schaften) durch kleine Temperatur- und Druckvariationen über große Bereiche verändert werden (s. Tab. 1). Dies kann alternative Reaktionswege eröffnen, d. h. die chemische Umgebung kann angepaßt werden, ohne daß man das Lösungsmittel Wasser wechseln muß. Eine Ursache ist die Veränderung der intermolekularen Wechselwirkung der Wassermoleküle (dreidimensionaler Wasserstoffbrückenverband) beim Übergang in den überkritischen Zustand.

Die industrielle Anwendung von superkritischem Wasser (SCW) beschränkte sich in der Vergangenheit vor allem auf die Zerstörung von schwer abbaubaren und toxischen Abfallstoffen mittels der „supercritical water oxidation“ (SCWO) [3, 4]. Um das Synthesepotential von SCW zu eruieren, wurden Hydratisierungs- und Dehydratisierungsreaktionen sowie Hydrolysen verschiedener Modellsubstanzen (Alkohole, Ester, Nitrile, Amide) im unter- und überkritischen Bereich ohne den Zusatz von Katalysatoren (Säuren, Basen) durchgeführt, um die Nachteile der „klassischen“ Reaktionsführung (u. a. Einsatz von Mineralsäuren und Salzanfall, geringe Raum-Zeit-Ausbeuten) zu überwinden. Die meisten Untersuchungen in SCW wurden bisher entweder in kleinen Autoklaven oder in Kapillarrohr-Reaktoren durchgeführt [5-7], so daß Wandeffekte des entsprechenden Reaktormaterials nicht immer auszuschließen sind. Aus diesem Grunde wurde für die Untersuchungen eine kontinuierliche Anlage mit „technischen“ Dimensionen aufgebaut, wobei als maximale Betriebsbedingungen 500 bar und 500 °C gewählt wurden, die für industrielle Anwendungen als realistische obere Grenzwerte anzusehen sind.

In diesem Artikel sollen die Versuchsanlage und die ersten Ergebnisse über die Reaktionen einfacher Modellsubstanzen mit überkritischem Wasser dargestellt werden.

2 Experimenteller Teil

2.1 Kontinuierliche Hochdruckapparatur

Zur Durchführung der Versuche in überkritischem Wasser wurde die in Abb. 1 schematisch dargestellte kontinuierliche Hochdruckapparatur aufgebaut. Das Kernstück der Anlage bilden zwei Rohrreaktoren aus Inconel 625 (10 ml bzw. 50 ml), die für folgende Betriebsbedingungen ausgelegt sind:

- Druck bis 50 MPa.
- Temperaturen bis 500 °C.

Tabelle 1.

Eigenschaften von Wasser unter verschiedenen Bedingungen [1, 2].

Fluid	normales Wasser	unterkritisches Wasser	überkritisches Wasser		überhitzter Dampf
			250 bar	500 bar	
Temperatur T [°C]	25	250	400	400	400
Druck p [bar]	1	50	250	500	1
Dichte ρ [g cm ⁻³]	1	0,89	0,17	0,55	0,604
Dielektrizitätskonstante	78,5	27,1	3,4	10,5	1,1
pK _s -Wert	14,0	11,0	14,4	11,9	
Wärmekapazität [kJ kg ⁻¹ K ⁻¹]	4,18	4,86	13,0	6,8	2,1
Dynamische Viskosität [mPa s]	0,89	0,11	0,03	0,07	0,02
Wärmeleitfähigkeit [mW m ⁻¹ K ⁻¹]	0,68	0,20	1,60	4,38	5,5

Ringspalt in Richtung der Kapillarsäule mitnimmt. Die Dauer dieser Schaltung legt die Menge der dosierten Probe fest. Im Anschluß an den Dosiervorgang wird die Glaskugel mit Stickstoff gespült (MV3) und ist für die nächste Injektion bereit. Für die Analysen wurde eine 50 m lange FFAP-Kapillarsäule (CHROMATOGRAPHIE-SERVICE GMBH, Innendurchmesser = 0,32 mm; Filmdicke = 0,25 µm) und Stickstoff bzw. Helium (GC-MS) als Trägergas verwendet; 1,4-Dioxan diente als interner Standard.

3 Ergebnisse

Die Versuche wurden, wenn nicht anders angegeben, unter folgenden Reaktionsbedingungen durchgeführt:

- 250 bar,
- 250 bis 400 °C,
- mittlere Verweilzeit 2 Minuten,
- Eingangskonzentration 5 % (g g⁻¹).

3.1 Dehydratisierung von 1,4-Butandiol

Die Wunschreaktion ist hier die Bildung von Tetrahydrofuran aus 1,4-Butandiol in SCW ohne den Zusatz eines sauren Katalysators, s. Abb. 3.

Abbildung 3.
Dehydratisierung von 1,4-Butandiol.



Abbildung 4.
Dehydratisierung von Glycerin.

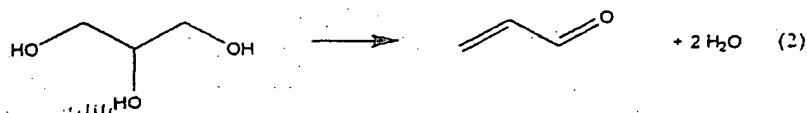


Abbildung 5.
Umsetzung von Acetoncyanhydrin.

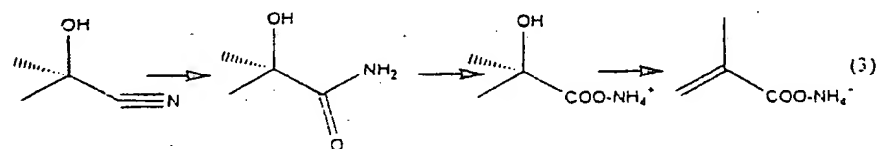


Abbildung 6.
Zersetzung von Acetoncyanhydrin.

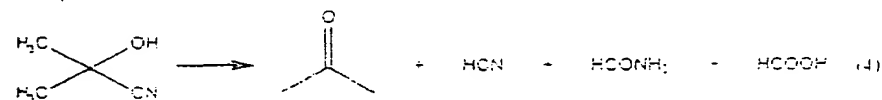


Abbildung 7.
Hydrolyse von Ethylacetat.



Ergebnis:

1,4-Butandiol läßt sich im nah- und überkritischen Wasser selektiv zu Tetrahydrofuran dehydratisieren. Es wurden keine weiteren Produkte nachgewiesen. Der Umsatz steigt mit der Temperatur stark an. Er beträgt bei 250 °C 5 % und erhöht sich auf 38 % bei 400 °C (2 min Verweilzeit).

Tetrahydrofuran ist unter den gewählten Reaktionsbedingungen stabil. Es wurden keine Zersetzungsprodukte gefunden.

3.2 Dehydratisierung von Glycerin

Die Wunschreaktion ist hier die Dehydratisierung von Glycerin in SCW zu Acrolein, s. Abb. 4.

Ergebnis:

Die Dehydratisierung von Glycerin zu Acrolein setzt erst ab einer Temperatur von 350 °C in merklichem Umfang ein. Die Umsetzung erfolgt hierbei selektiv zu Wasser und Acrolein. Es wurden keine weiteren Produkte gefunden.

3.3 Umsetzung von Acetoncyanhydrin

Die Wunschreaktion ist hier die Bildung von Methacrylsäure, über eine Verseifung der Nitrilgruppe und anschließender Wassereliminierung der α-Hydroxybuttersäure, s. Abb. 5.

Ergebnis:

Das gewünschte Produkt konnte nicht nachgewiesen werden. Es erfolgt im nah- und überkritischen Wasser eine Zersetzung des Acetoncyanhydrins zu Aceton, Blausäure, Formamid und Ameisensäure, s. Abb. 6.

3.4 Hydrolyse von Ethylacetat

Die Verseifung von Ethylacetat (stellvertretend für alle Ester) wurde unter erweiterten Reaktionsbedingungen (250 bis 400 °C, 23 bis 30 MPa) und unter Variation der Verweilzeit durchgeführt. Erwünscht ist eine selektive Umsetzung zu Essigsäure und Ethanol ohne den Zusatz von basischen bzw. sauren Katalysatoren, s. Abb. 7.

Ergebnis:

Als Produkte der Hydrolyse wurden bei allen Versuchen in der Flüssigphase nur Essigsäure und Ethanol gefunden, erst oberhalb von 350 °C sind geringe Mengen an Ethylen, CO und CO₂ in der Gasphase nachweisbar. Der größte Umsatz im Temperaturbereich von 250 bis 400 °C wird bei allen untersuchten Drücken bei 350 °C, d. h. kurz unterhalb des kritischen Punktes von Wasser, erzielt (s. Abb. 8).

weniger von der Temperatur abhängig. Neben Essigsäure wird auch in geringen Mengen Acetonitril gebildet.

4 Schlußbetrachtung

Die Versuche haben gezeigt, daß viele Hydratisierungs- und Dehydratisierungsreaktionen sowie Hydrolysen ohne zusätzliche Hilfsstoffe, wie Säuren oder Basen, in überkritischem Wasser hochselektiv und mit hohen Raum-Zeit-Ausbeuten ablaufen. Allerdings werden komplexere Verbindungen, wie z. B. Acetoncyanhydrin, in SCW zersetzt.

- Die Hydrolyse von 1,4-Butandiol in SCW verläuft selektiv zu Tetrahydrofuran, wobei Tetrahydrofuran nicht weiter reagiert.
- Ab einer Temperatur von 350 °C dehydratisiert Glycerin zum erwünschten Produkt Acrolein.
- Essigsäureethylester (stellvertretend für alle Ester) läßt sich in SCW selektiv zu Essigsäure und Ethanol verseifen.
- Acetonitril wird in SCW in einer einfachen Folgereaktion selektiv zu Acetamid bzw. Essigsäure hydrolysiert.
- Die Umsetzung von Acetamid in SCW liefert überwiegend Essigsäure, nur ein geringer Teil wird zu Acetonitril dehydratisiert.

Bei allen Versuchen zeigte sich, daß die Reaktionsgeschwindigkeit von vielen Faktoren abhängt. Da die Effekte sich teilweise gegenläufig verhalten, lassen sich über die Reaktionskinetik in SCW keine a priori Aussagen machen. Um die erhaltenen Ergebnisse zu erklären und mit den Eigenschaften des SCW zu korrelieren, sind weitere detaillierte kinetische Untersuchungen erforderlich.

Die Autoren danken der BASF Aktiengesellschaft, Ludwigshafen, für die finanzielle Unterstützung dieser Arbeit.

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Literatur

- [1] TÖDHEIDE, K.
in: F. Franks: Water - A Comprehensive Treatise.
N.Y. 1972.
- [2] HAAR, L.; GALLAGHER, J. S.; KELL, G. S.
NBS/NRC Steam Tables, Hemisphere, Washington
D.C. 1984.
- [3] GLOYNA, E. F. U. L.
Environ. Prog. 14 (1995) S 182
- [4] SPRITZER, M. H.; HAZLEBECK, D. A.; DOWNEY, K. W.
J. Energ. Mater. 13 (1995) S 185.
- [5] TORRY, L. A.; KAMINSKY, R.; KLEIN, M. T.; KIRTEL, M. R.
J. Supercrit. Fluids 5 (1992) S 163
- [6] WEST, M. A. B.; GRAY, M. A.
Can. J. Chem. Eng. 65 (1987) S 645
- [7] SAVAGE, P. E.; GOPALAN, S.; MEYER, L. J.; MARTINO, C. J.
Environ. Prog. 14 (1995) S 171
- [8] Analysetechnik BEHRENDT
Analysetechnische Informationen 1. Mainz-Ka-
stel 1993
- [9] LARSON, K. J.
in: Chemical Kinetics, Third Edition, Harper & Row
Publishers, New York 1987

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Eignen sich Nickel-Trägerkatalysatoren für die partielle Gasphasenhydrierung von Benzol zu Cyclohexen?

p. d. 12-1998

ENRICO DIETZSCH, UTE RYMSA UND DIETER HONICKE

Herrn, Professor Dr.-Ing. GERHARD EMIG zum 60. Geburtstag.

Infolge der Verminderung des Benzol-Anteils in Fahrbenzinen und der angestrebten vollständigen Substitution desselben durch umweltschonendere Antiklopffmittel wird die Frage nach der chemischen Verwendung des Benzols zunehmend gestellt werden. Eine partielle Hydrierung des Benzols zum Cyclohexen, anstatt wie weitestgehend praktiziert zum Cyclohexan, ist vom Standpunkt der Petrochemie eine interessante Aufgabe. Ausgehend vom Cyclohexen sind über olefintypische Reaktionen eine ganze Reihe von interessanten Wertprodukten, wie z. B. Cyclohexanol, ϵ -Caprolactam und Adipinsäure, zugänglich. Ein erster technisch etablierter Prozeß nutzt die katalytische Aktivität von Ruthenium zur partiellen Benzolhydrierung in der Flüssigphase [1]. Auch partielle Benzolhydrierungen in der Gasphase wurden unter Verwendung dieser Aktivkomponente untersucht [2, 3]. Die dabei dokumentierten Cyclohexen-Ausbeuten sind jedoch ungleich geringer als in der Flüssigphasenhydrierung, so daß für diesen Bereich noch erheblicher Untersuchungsbedarf besteht.

1 Problemstellung

Die Besonderheiten des Reaktionssystems (s. Abb. 1) sind seit langem bekannt. Aus thermodynamischen Gründen findet eine Hydrierung des Benzols nur bei niedrigen Temperaturen statt. Ausschließliches Produkt sollte in diesem Falle der gesättigte Kohlenwasserstoff Cyclohexan sein. Betrachtet man die kinetischen Gesichtspunkte, so wirken einerseits die Reaktionsträgheit des Aromaten Benzols und andererseits die hohe Reaktivität des Cyclohexens einer partiellen Hydrierung des Benzols unter bevorzugter Cyclohexenbildung entgegen. Dennoch gibt es inzwischen zahlreiche Dokumentationen, in denen Ruthenium-Katalysatoren zur partiellen Gasphasenhydrierung von Benzol herangezogen wurden. Kriterium für die Cyclohexen-Bildung ist dabei das Vorhandensein eines Reaktionsmodifiziers in der Gasphase, welcher in das Adsorptions- und Stofftransportgeschehen eingreift [2, 3].

Abbildung 1.
Reaktionsschema bei der partiellen Hydrierung von Benzol in der Gasphase.



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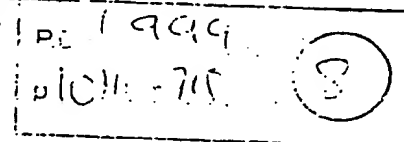
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The Continuous Acid-Catalyzed Dehydration of Alcohols in Supercritical Fluids: A New Approach to the Cleaner Synthesis of Acetals, Ketals, and Ethers with High Selectivity

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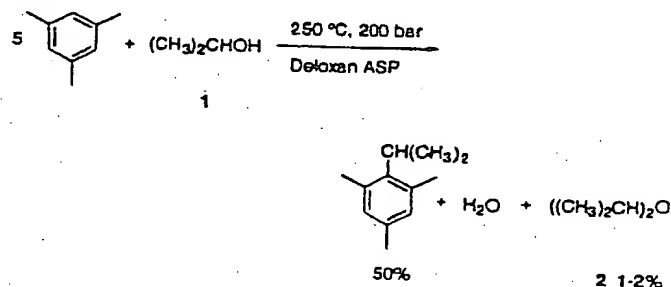
Abstract: We report a new continuous method for forming ethers, acetals and ketals using solid acid catalysts: DELOXAN ASP or AMBERLYST 15, and supercritical fluid solvents. In the case of ether formation, we observe a high selectivity for linear alkyl ethers with little rearrangement to give branched ethers. Such rearrangement is common in conventional syntheses. Our approach is effective for a range of *n*-alcohols up to *n*-octanol and also for the secondary alcohol 2-propanol. In the reaction of phenol with an alkylating agent, the continuous reaction can be tuned to give preferential O- or C-alkylation with up to 49% O-alkylation with supercritical propene. We also investigate the synthesis of a range of cyclic ethers and show an improved method for the synthesis of THF from 1,4-butanediol under very mild conditions.

Introduction

In recent years there has been an increasing interest in environmentally more sustainable chemical processes.^{1,2} This has led to increased research into the use of supercritical fluids (SCFs),³⁻⁵ especially carbon dioxide, *sc*CO₂, as an environmentally benign and economically feasible reaction medium for heterogeneously catalyzed reactions.^{3,4,6}

SCFs are gases heated above their critical temperature (*T_c*) and compressed above their critical pressure (*P_c*).^{7,8} CO₂ has a critical point close to ambient temperature (*T_c* = 31.3 °C, *P_c* = 72.9 atm)⁴ and is nonflammable, nontoxic, and inexpensive. With extremely low viscosity and good thermal and mass transport properties, SCFs are attractive solvents for continuous reactions. Moreover, their properties can be tuned within certain limits by adjusting pressure and temperature (and hence the density). In a continuous flow reactor, such parameters can be adjusted independently, giving very precise control over reaction conditions. Furthermore, continuous reactors are generally smaller and safer than batch reactors with equivalent production capacity.⁹

Scheme 1



We have previously reported^{10,11} how SCFs, particularly *sc*CO₂, can be used for the continuous hydrogenation of a wide range of organic substrates using a fixed-bed reactor packed with a supported noble metal catalyst (e.g. Pt, Pd, etc.). This supercritical process combines cleaner processing with very high conversions and high product selectivities. More recently, with slightly modified equipment, we have carried out selective Friedel-Crafts alkylation reactions using solid acid catalysts and alcohols as the alkylating agents.¹² In some of these alkylation reactions, we observed small amounts of ethers as byproducts, formed by condensation of two molecules of the alcohol, Scheme 1. It was this observation which prompted the study of etherification in *sc*CO₂, reported here.

Acid-Catalyzed Reactions in the Supercritical Phase. A greater number of fundamental catalytic organic reactions are promoted by acid than all other catalytic reactions added together.^{13,14} Solid acid catalysts such as clays, zeolites and even

[†] University of Nottingham. Internet: <http://www.nottingham.ac.uk/supercritical>

[‡] Thomas Swan and Co. Ltd.

(1) Anastas, P. T.; Williams, T. C. *Green Chemistry: Designing Chemistry for the Environment*; Oxford University Press: Oxford, 1998.

(2) Anastas, P. T.; Warner, J. C. *Green Chemistry: Theory and Practice*; Oxford University Press: Oxford, 1998.

(3) Savage, P. E. *Chem. Rev.* 1999, 99, 603.

(4) Baiker, A. *Chem. Rev.* 1999, 99, 453.

(5) Dart, J. A.; Poliakoff, M. *Chem. Rev.* 1999, 99, 495.

(6) Savage, P. E.; Gopalan, S.; Mizan, T. I.; Martino, C. J.; Brock, E. E. *AIChE J.* 1995, 41, 1723.

(7) Eckert, C. A.; Kautson, B. L.; Debendani, P. G. *Nature* 1996, 383, 313.

(8) McHugh, M. A.; Krukowski, V. J. *Supercritical Fluid Extraction: Principles and Practice*; Butterworth-Heinemann: Boston, 1994.

(9) Tundo, P. *Continuous Flow Methods in Organic Synthesis*; Ellis Horwood: Chichester, UK, 1991.

(10) Hitzler, M. G.; Poliakoff, M. *Chem. Commun.* 1997, 1667.

(11) Hitzler, M. G.; Small, F. R.; Ross, S. K.; Poliakoff, M. *Org. Process Res. Dev.* 1998, 2, 137.

(12) Hitzler, M. G.; Small, F. R.; Ross, S. K.; Poliakoff, M. *Chem. Commun.* 1998, 359.

(13) Ertl, G.; Knozinger, H.; Weitkamp, J. *Handbook of Heterogeneous Catalysis*; Wiley-VCH: Weinheim, 1997; Vol. 5.

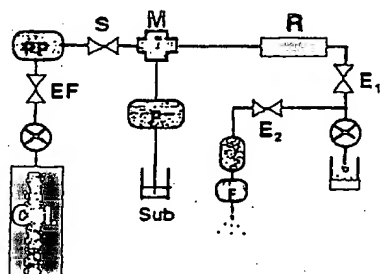


Figure 1. Schematic view of the apparatus used for etherification. The parts are labeled as follows (alphabetically): Cyl, cylinder of gas (CO_2 , propane or propene); EF, excess flow cut-out valves; E_1 and E_2 , two expansion valves for pressure reduction and flow control; F, flow meter; M, mixer; P, HPLC pump (0.3–20.0 mL/min, Gilson model 303); PP, pneumatic pump 20–200 atm (module PM 101, NWA GmbH); Prod, product(s); R, reactor made from 316 stainless steel tubing (9 mm i.d.), length 152 mm or 304 mm (10 mL or 20 mL volume respectively), containing the solid catalyst; S, regulator which determines the system pressure; Sub, organic substrate; T, trap for any droplets inadvertently carried through with the gas (CO_2 , propane or propene).

the appropriate pressure rating. It is the responsibility of individual researchers to verify that their particular apparatus meets the necessary safety requirements. The components described below work well, but they are not necessarily the only equipment of this type available nor the most suitable for the purpose.

Figure 1 shows the apparatus used in these experiments, which is similar to that used for hydrogenations¹¹ but without an H_2 supply. The gaseous solvent (CO_2 , propane, or propene) is pressurized using the pneumatic pump, PP, and then reduced to system pressure across valve S. The solvent enters the mixing area, M, where it meets the organic substrate, the mixture then passes through the reactor, R, containing the catalyst. After the fluid passes through the reactor, the pressure is dropped stepwise to separate the product(s) from the fluid using an expansion module (PE 103, NWA GmbH). In this module, the expansion valve E_2 controls the flow rate of the exhaust gases. Additionally, a flow meter, F, measures the flow rate of the fluid, which is typically set to 0.65 L/min of gas at 1 atm and 20 °C, corresponding to 1.06 g of CO_2 /min. The organic products are recovered free of any solvent and thus they can immediately be analyzed by NMR (Bruker DPX 300), GC (Philips PU 4500), or GC-MS (Shimadzu QP-5000) without further workup.

R is heated by three cartridge-heaters in an aluminum block, which encases the reactor. The heaters are thermostatically controlled by a thermocouple reading the temperature of the catalyst bed. Two additional thermocouples are used to monitor the system, one reading the temperature of the Al heating block and the other in the fluid stream at the end of the reactor. For all of the reactions described in this paper, the temperature quoted is that of the catalyst bed.

We have used two types of solid acid catalyst in the experiments described here. DELOXAN ASP catalyst (Degussa-Huls AG, Frankfurt, Germany) has in the past been found¹² to be a reliable and convenient catalyst for use in our continuous flow reactor. During the course of our study, we have also found that AMBERLYST resin-based acid catalysts (Rohm and Haas Co.) can also be effective. All reactions described in this paper were run with commercially available substrates (Aldrich, Fluka, Acros). The apparatus used in these experiments gave a high degree of reproducibility.

Results and Discussion

Cyclic Ether Formation. Synthesis of Tetrahydrofuran (4) from 1,4-Butanediol (3). Our preliminary investigations into ether formation have been carried out using the cyclization of 1,4-butanediol, 3, to THF, 4, as a model reaction, because it is both facile and clean and has no unwanted byproducts (see Scheme 2). Furthermore, the cyclization of 3 is also a significant industrial route to 4, with more than 50% of 3 produced annually

Scheme 2

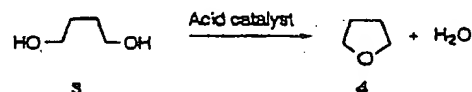


Table 1. Effect of Reactor Conditions on the Conversion of 3 into 4 in scCO_2 ^a

	temperature (°C)	pressure (atm)	flow rate of 3 (mL/min)	product	
				4 (%) ^b	3 (%)
varying T	100	100	0.5	63	37
	125	100	0.5	96	4
	150	100	0.5	100	0
	175	100	0.5	100	0
	200	100	0.5	100	0
varying P	100	125	0.5	69	31
	100	150	0.5	79	21
	100	175	0.5	81	19
	100	200	0.5	87	13
	150	60–200	0.5	100	0
varying flow rate of 3	150	100	0.5	100	0
	150	100	1.0	100	0
	150	100	2.0	98	2
	150	100	3.0	93	7

^a Other reaction conditions: DELOXAN ASP catalyst; 10 mL reactor; flow rate of CO_2 0.65 L/min. ^b In all tables presented in this paper the symbol (%) next to a numerical identifier refers to the percentage yield of that particular product, as found upon analysis of the material collected.

in USA being used in the manufacture of THF.¹⁴ Conventionally, 3 is passed through a hot tube in the presence of H_2SO_4 or H_3PO_4 at 100 atm and 300 °C, with 4 being generated in 90–100% yield in a continuous process.

For our experiments 3 (mp 16 °C) was first dissolved in a small amount of MeOH, (25 g 3 in 10 mL) to ensure that 3 did not solidify in any of the pipework. The cyclization of 3 in scCO_2 is highly successful. Flow rates of up to 1.0 mL/min of 3 can be maintained for up to 15 h over the same catalyst with no loss of activity. Table 1 shows the effect of temperature and pressure on the yield of 4. Thus, increasing the reactor temperature from 100 to 125 °C at 100 atm results in a 33% increase in the yield of 4, and increasing it to 150 °C gives full conversion. At 150 °C, varying the pressure inside the reactor had no effect on conversion, even at only 60 atm (below the critical pressure of CO_2).⁴³ However, at 100 °C, a clear relationship between reactor pressure and yield can be seen, with an 18% increase in conversion when the pressure was raised from 100 to 200 atm. Such an effect is to be expected, considering that, in fixed bed flow reactors and under these conditions, an increase in pressure, at constant temperature, increases the residence time of the substrate over the catalyst. It should be noted that under steady state conditions the weight hourly space velocity of material passing through our apparatus will remain the same irrespective of the system pressure. However, the residence time over the catalyst will be affected by pressure because of the high compressibility of the supercritical fluid.

Etherification of 1,5-Pentanediol (5) and 1,6-Hexanediol (8). 5 and 8 can be dehydrated with very high selectivity for tetrahydropyran, 6, and the oxepane ring, 9, respectively (see Table 2). This is a striking result since one would generally expect the rearranged 2-alkyltetrahydrofurans, 7 and 10, to

(43) 60 atm is above the vapor pressure of CO_2 at room temperature. Thus, under these conditions liquid CO_2 will mix with the reactant(s) in the cool part of the apparatus upstream of the reactor. Thus CO_2 /reactant mixtures is likely to be formed.

the corresponding *n*-alcohols over the DELOXAN ASP catalyst in scCO_2 . For all alcohols, the yields in a 20 mL reactor were significantly higher than those in a 10 mL vessel, with little effect on selectivity.

Poor yields were obtained for *n*-octanol, 30, which is dehydrated readily under these conditions to give octene, probably as a result of the reduced solubility of long chain alcohols in scCO_2 .⁵¹ The reaction between *n*-BuOH, 24, and MeOH is interesting because, even when a 2.5:1 excess of MeOH is used, *n*-Bu₂O, 25, and *n*-BuOMe, 33, are produced in *comparable amounts*, rather than the expected large excess of 33. This suggests either that MeOH must be forming its corresponding cation *less readily* than 24 or that 33 may possibly be formed via trans-etherification of Me₂O with 24.

In all of the reactions of *n*-alcohols, we observed some alkene production, resulting from the competing dehydration process, with significant amounts only occurring when high temperatures were used (typically above 200 °C in the 10 mL reactor). Usually the predominant olefin product is the corresponding 2-alkene, although some 1-alkene is observed. Production of these olefins causes the yield of, and the selectivity for, the *n*-ether to fall because Markovnikov protonation of the olefin will result in formation of a secondary carbocation, leading to branched ethers. For this reason, it is important to maintain a balanced temperature. Pressure effects in these reactions are similar to those already observed for the formation of cyclic ethers, acetals, and ketals and is likely to be due to the same reasons (i.e., longer residence time and the negative volume of activation for bimolecular reactions).

Origin of the High Selectivity for *n*-Ethers: Solvent Effects. To establish whether scCO_2 itself affects the selectivity, a number of experiments were carried out in supercritical propane (scPropane ; $T_c = 96.6$ °C, $P_c = 41.9$ atm).⁴ The results, Table 5, suggest that scCO_2 is a better solvent than scPropane for these reactions, although it is not yet clear why. Possibly, the ether products are more soluble in scCO_2 than in scPropane and, thus are more efficiently separated from H₂O, thereby avoiding a back reaction.⁵¹ It should be noted that in a flow reactor it is difficult to make precise comparisons between two supercritical fluids because some of the reaction parameters will usually be different. For example, at 200 °C and 200 atm the density of CO₂ (0.2629 g/mL) is lower than that of propane (0.3145 g/mL) at the same temperature and pressure.⁵⁵ To match the fluid densities inside the reactor, the pressure during the scPropane experiment could be lowered, but this might decrease the residence time of the reactants inside the reactor, making a quantitative comparison between CO₂ and propane more difficult.

The supercritical solvent appears to play a definite role in determining the yield, but not the selectivity. Thus when *n*-PrOH, 21, was passed over the catalyst in the flow reactor at 200 °C and 200 atm *without any supercritical fluid*, it gave predominantly the *n*-Pr₂O, although in a yield (7% 22:4% 23) much lower than that with scCO_2 . Similarly, when *n*-hexanol, 27, was refluxed (~156 °C) over DELOXAN ASP in the absence of any solvent (but with the possibility of H₂O venting off), *n*-hexyl ether, 28, (12.5% after 2 h) was formed much more slowly than in our flow reactor, but with only 1% of the branched ether, 29. This selectivity is similar to that obtained in the flow reactor.

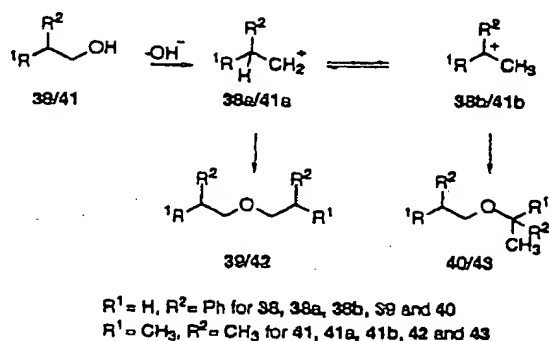
Effect of Catalyst: Comparison of DELOXAN ASP with AMBERLYST 15. DELOXAN ASP was used as the catalyst

Table 4. Continuous Formation of Acyclic Ethers in scCO_2 ^a

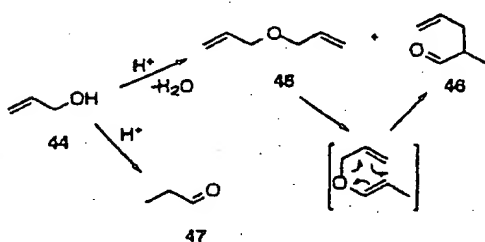
substrate	T (°C)	reactor size (mL)	products ^{b,c}		
			(<i>n</i> -Pr) ₂ O 22 (%)	<i>n</i> -PrO <i>i</i> -Pr 23 (%)	alkene/rearranged alcohol (%)
<i>n</i> -PrOH 21	200	10	29	4	5
	150	20	60	8	10
substrate	T (°C)	reactor size (mL)	products ^{b,c}		
			(<i>n</i> -Bu) ₂ O 25 (%)	<i>n</i> -BuO <i>i</i> -Bu 26 (%)	alkene/rearranged alcohol (%)
<i>n</i> -BuOH 24	200	10	33	1	5
substrate	T (°C)	reactor size (mL)	products ^{b,c}		
			(<i>n</i> -C ₆ H ₁₃) ₂ O 28 (%)	<i>n</i> -C ₆ H ₁₃ O <i>i</i> -C ₆ H ₁₃ 29 (%)	alkene/rearranged alcohol (%)
<i>n</i> -C ₆ H ₁₃ OH 27	200	10	34	1	11
	150	20	54	8	16
substrate	T (°C)	reactor size (mL)	products ^{b,c}		
			(<i>n</i> -C ₈ H ₁₇) ₂ O 31 (%)	<i>n</i> -C ₈ H ₁₇ O <i>i</i> -C ₈ H ₁₇ 32 (%)	alkene/rearranged alcohol (%)
<i>n</i> -C ₈ H ₁₇ OH 30	150	10	14	0	10
	200	10	0	0	95
substrate	T (°C)	reactor size (mL)	products ^{b,c}		
			(<i>n</i> -Bu) ₂ O 25 (%)	<i>n</i> -BuO <i>i</i> -Bu 26 (%)	<i>n</i> -Bu-O-Me 33 (%)
<i>n</i> -BuOH + MeOH 24 ^d	200	10	24	1	27
1:2.5					
substrate	T (°C)	reactor size (mL)	products ^{b,c}		
			(<i>n</i> -Bu) ₂ O 25 (%)	<i>n</i> -BuO <i>n</i> -Pr 34 (%)	alkene/rearranged alcohol (%)
<i>n</i> -BuOH + <i>n</i> -PrOH 24 ^d + 21	200	10	20	28	9
1:1.2					
substrate	T (°C)	reactor size (mL)	products ^{b,c}		
			(<i>n</i> -Pr) ₂ O 22 (%)	<i>n</i> -PrO <i>i</i> -Pr 23 (%)	alkene/rearranged alcohol (%)
<i>n</i> -PrOH + <i>i</i> -PrOH 21 ^d + 1	150	20	12	41	7
1:1.2					
substrate	T (°C)	reactor size (mL)	products ^{b,c}		
			PhCH ₂ OMe 36 (%)	<i>p</i> -PhCH ₂ -C ₆ H ₄ -CH ₂ OH 37 (%)	
PhCH ₂ OH + MeOH 35 ^d	200	10	84	7	
1:2.5					
substrate	T (°C)	reactor size (mL)	products ^{b,c}		
			(Ph(CH ₂) ₂) ₂ O 39 (%)	Ph(CH ₂) ₂ -O-CH(CH ₃)Ph 40 (%)	
Ph(CH ₂) ₂ OH 38	200	10	58	2	
substrate	T (°C)	reactor size (mL)	products ^{b,c}		
			(<i>i</i> -Bu) ₂ O 42 (%)	<i>i</i> -BuO <i>i</i> -Bu 43 (%)	alkene/rearranged alcohol (%)
<i>i</i> -BuOH 41	200	10	8	5	5
substrate	T (°C)	reactor size (mL)	products ^{b,c}		
			(CH ₃ =CHCH ₂) ₂ O 45 (%)	CH ₃ =CHCH ₂ -CH(CH ₃)CHO 46 (%)	
CH ₃ =CHCH ₂ OH 44	60	10	1	0	
	120	10	9	1 ^e	

^a Other reaction conditions: DELOXAN ASP catalyst; 200 atm; flow rates = CO₂ 0.65 L/min, substrate 0.5 mL/min. ^b All material not accounted for was recovered as unreacted starting material. ^c Yields of volatile alkenes (propene, butene, etc.) were calculated by mass balance. ^d Yields based on 24 consumed; 5% alkene/rearranged alcohol products also formed. ^e Yields based on 24 consumed; yield of 22 (formed as a result of self-condensation of 21) was 13%, based on 21 consumed; 4% mixed branched ether products also formed. ^f Yields based on 21 consumed; yield of 2 (formed as a result of self-condensation of 1) was 60%.

Scheme 4



Scheme 5



the acid/substrate interaction.^{45,59,60} Finally, although we observe no carbonate species resulting from reaction of CO_2 with the alcohol in the product mixture, we cannot rule out the formation of such species as transient intermediates in the reactions carried out in scCO_2 .

2-Phenyl-1-ethanol (38) and Isobutanol (41). Table 4 also shows that there is a high selectivity (12:1) for the *n*-terminal product, 39, in the etherification of 38. This selectivity is striking because the rearranged benzylic cation, 38b, is stabilized by the adjacent aromatic ring and thus is much more stable than the secondary cation, 38a, and hence, rapid rearrangement would be expected under normal reaction conditions, see Scheme 4.

Tertiary cations are, in turn, more stable than benzylic cations, and this may explain why *i*-BuOH (2-methylpropanol), 41, gave a much lower (8:5) *n*-ether selectivity, with rapid formation of the rearranged *tert*-butyl cation, 41b, and consequent formation of ether 43, see Table 4 and Scheme 4.

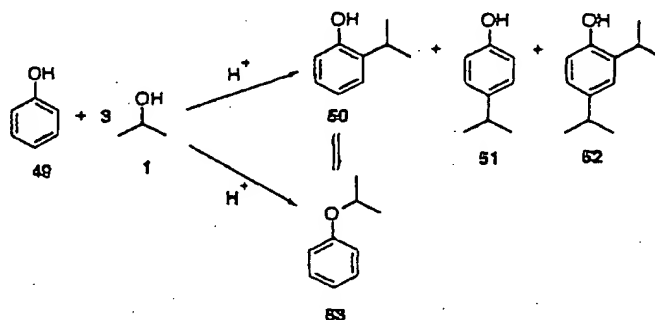
Allyl Alcohol (44). Table 4 shows that the etherification of 44 was an unsuccessful reaction, even in scCO_2 . In this reaction, propanal, 47, is formed by a simple rearrangement of the double bond. The other aldehyde product, 46, arises from rearrangement of one of the double bonds in the ether, 45, followed by a Claisen-type sigmatropic rearrangement (see Scheme 5).

Reaction of Secondary Alcohols. *i*-PrOH, 1, is the only secondary alcohol that can be dehydrated to give an ether in our system (29% yield at 200 °C). Even so, propene was the major reaction product (56%). At temperatures above 200 °C, propene was formed in >80% yield, with a corresponding decrease in the yield of ether 2. Surprisingly, the yield of 2 also decreased when a 20 mL reactor was used, instead of 10 mL, under identical conditions. Reaction of longer chain secondary alcohols, such as *s*-pentanol, 48, gave exclusively alkenes with no evidence for any ether formation, even at reduced temperatures. Clearly, secondary alcohols, apart from 1, cannot be etherified effectively in our system due to the ease with which they dehydrate.

(59) Angeletti, E.; Canepa, C.; Marinetti, G.; Vennurello, P. *Tetrahedron Lett.* 1988, 2261.

(60) Angeletti, E.; Canepa, C.; Marinetti, G.; Vennurello, P. *J. Chem. Soc., Perkin Trans. 1* 1989, 29, 105.

Scheme 6



Aryl Ethers. We have previously reported that the Friedel–Crafts alkylation of mesitylene and anisole can be carried out with 1 in our flow reactor.¹² When phenol, 49, is used as the substrate, competing etherification and alkylation reaction should occur, as shown in Scheme 6. Conventionally, selective etherification of phenol (O-alkylation) can be difficult to achieve. Although many authors have studied such reactions,^{48,49,61–72} there is still a degree of confusion over exactly which factors favor O-alkylation versus C-alkylation. Although it is agreed that increasing reaction temperatures favor C-alkylation because of the thermodynamics of the process, the role of the catalyst is much less clearly defined. It has been claimed that the presence of strongly acidic sites on metal oxides, phosphates, and sulfates favors O-alkylation and, conversely, that weakly acidic sites favor C-alkylation. Zeolites also seem to have a similar effect, although Marczewski⁶⁴ has observed that strong acid sites on zeolite USHY favor both O- and C-alkylation to give cresols, while weak acid sites give only O-alkylation. More recently⁶¹ a high potassium content (3%) in sulfates has been claimed to give aryl ethers in excellent yields and selectivities (>90%).

We have studied the alkylation of 49 with 1 in scCO_2 , and with scPropene , at a variety of temperatures and pressures. When 1 was used as the alkylating agent, a 3:1 molar excess of 1:49 was used. When scPropene acting both as solvent and reagent was used, a 230:1 excess of propene was present. The results (Table 8 and Figure 2) indicate that reaction conditions can be manipulated to give a good degree of selectivity for etherification over Friedel–Crafts alkylation.

When 1 was used as the alkylating agent, the yield of *i*-PrOPh 53 reached a maximum of 32% at 160 °C and 160 atm. At this point the combined total of the Friedel–Crafts products 50, 51, and 52 was 13%. At 200 °C the yield of 53 is very low, and the dialkylated product predominates. In the Friedel–Crafts alkylation process, there is a high degree of selectivity for ortho-

(61) Samolada, M. C.; Grigoriadou, E.; Kiparissides, Z.; Vasalos, I. A. *J. Catal.* 1995, 152, 52.

(62) Sartori, G.; Bigi, F.; Maggi, R.; Arienti, A. *J. Chem. Soc., Perkin Trans. 1* 1997, 257.

(63) Marczewski, M.; Perot, G.; Perot, M. *Heterogeneous Catalysis and Fine Chemicals*; Elsevier: Amsterdam, 1988.

(64) Marczewski, M.; Bodido, J. P.; Perot, G.; Perot, M. *J. Mol. Catal.* 1989, 50, 211.

(65) Campelo, J. M.; Garcia, A.; Marinias, J. M.; Moreno, M. S. *Bull. Soc. Chim. Paris* 1988, 2, 283.

(66) Balsama, S.; Beltrame, P.; Beltrame, P. L.; Carmitti, P.; Forai, L.; Zuretti, G. *Appl. Catal.* 1984, 13, 161.

(67) Pierantozzi, R.; Nordquist, A. F. *Appl. Catal.* 1986, 21, 263.

(68) Yamanaka, T. *Bull. Chem. Soc. Jpn.* 1976, 49, 2669.

(69) Bezouhanova, C.; Al-Zihari, M. A. *Appl. Catal.* 1992, 83, 45.

(70) Santacesaria, E.; Grosso, D.; Gelosa, D.; Carra, S. *Appl. Catal.* 1990, 64, 83.

(71) Olah, G. A.; Kaspi, J.; Bukala, J. *J. Org. Chem.* 1977, 42, 4187.

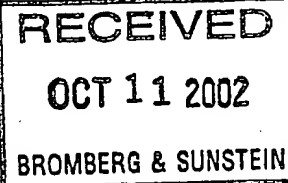
(72) Parلمان, R. A. U.S. Patent 4,299,996, 1981.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)



Applicant's or agent's file reference HL 71375/002	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/GB 00/ 00673	International filing date (day/month/year) 25/02/2000	(Earliest) Priority Date (day/month/year) 04/03/1999
Applicant THOMAS SWAN & CO. LTD. et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the language, the International search was carried out on the basis of the International application in the language in which it was filed, unless otherwise indicated under this item.

☐ the International search was carried out on the basis of a translation of the International application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any nucleotide and/or amino acid sequence disclosed in the International application, the International search was carried out on the basis of the sequence listing:

☐ contained in the International application in written form.

☐ filed together with the International application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the International application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

2. ☐ Certain claims were found unsearchable (See Box I).

3. ☐ Unity of invention is lacking (see Box II).

4. With regard to the title,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the abstract,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this International search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 00/00673

A. CLASSIFICATION OF SUBJECT MATTER

C 7 C07C41/09 C07C41/50 C07C1/20

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07C

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 831 116 A (WILLEY RONALD J ET AL) 3 November 1998 (1998-11-03) the whole document	1-16
A	EP 0 652 202 A (JAPAN RES DEV CORP ; IKARIYA TAKAO (JP)) 10 May 1995 (1995-05-10) page 3 -page 4	1-16
A	P. KRAMMER ET AL: "Untersuchungen zum Synthesepotential in überkritischem Wasser" CHEMIE INGENIEUR TECHNIK, vol. 70, no. 12, 1998, pages 1559-1563, XP000791730 Weinheim page 1561 -page 1562	1-16
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Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents:

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Date of the actual completion of the international search

23 May 2000

Date of mailing of the international search report

07/06/2000

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Authorized officer

Arias-Sanz, J

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 00/00673

C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

A	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	GRAY, WILLIAM K. ET AL: "The Continuous Acid-Catalyzed Dehydration of Alcohols in Supercritical Fluids: A New Approach to the Cleaner Synthesis of Acetals, Ketals, and Ethers with High Selectivity" J. AM. CHEM. SOC. (1999), 121(46), 10711-10718 , XP000887316 page 10711; tables 2-6 -----	1-16

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 00/00673

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
US 5831116	A	03-11-1998	NONE		
EP 0652202	A	10-05-1995	JP 2927677	B	28-07-1999
			JP 7330666	A	19-12-1995
			JP 2962649	B	12-10-1999
			JP 7330698	A	19-12-1995
			CA 2135138	A	05-05-1995
			DE 69403610	D	10-07-1997
			DE 69403610	T	18-12-1997
			DK 652202	T	22-12-1997
			JP 2774076	B	09-07-1998
			JP 7173098	A	11-07-1995
			US 5639910	A	17-06-1997
			US 5763662	A	09-06-1998
			US 5869739	A	09-02-1999